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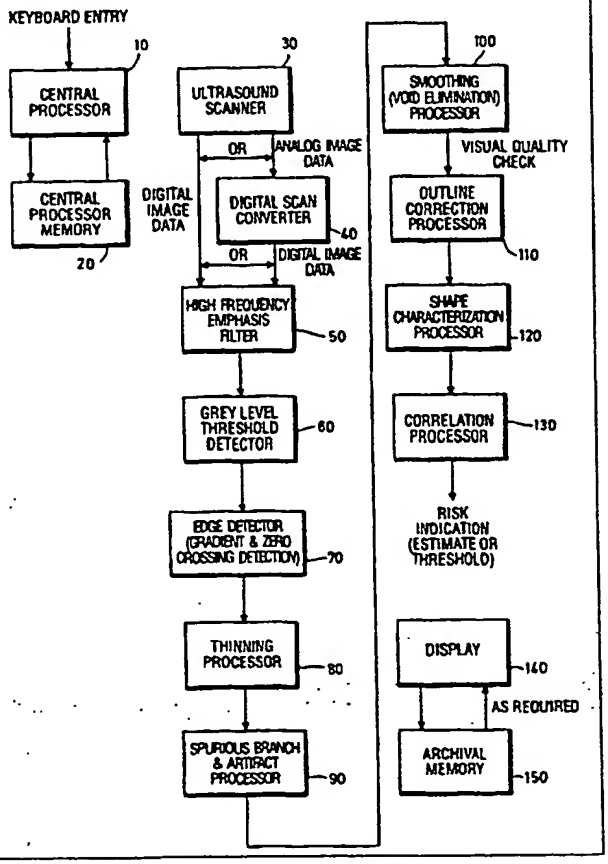
(57) Abstract

Non-invasive medical scanning apparatus comprises scanning means for non-invasively generating an image of at least an interior region of a subject to be examined; and means for detecting a quantitative measure indicative of the shape of the image, the quantitative measure having a correlation with the presence of a medical abnormality in that subject.



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NON-INVASIVE MEDICAL SCANNING

BACKGROUND OF THE INVENTION

Field of the Invention

This invention relates to non-invasive medical scanning.

Description of the Prior Art

Non-invasive medical scanning, such as ultrasound scanning, is used in the imaging of the interior of the human body. In the case of ultrasound scanning, ultrasonic vibrations generated by a hand-held transducer are transmitted into the body through the skin or mucous membranes, and are reflected back to the transducer from tissues of different densities within the body. As described in the book "Physics and Instrumentation of Diagnostic Medical Ultrasound" (P. Fish, John Wiley & Sons, 1990), an image of a cross-section through the body can be built up by analysing the relative amplitudes and delays of the reflected vibrations.

One particular use which has been made of ultrasound scanning is the examination of the fetus in the mother's uterus. A skilled operator can determine the orientation, gestational age and general condition of the fetus from its ultrasound image. Also, some fetal abnormalities, such as cardiac or renal abnormalities, can be diagnosed by the operator. A difficulty is that some fetal abnormalities which would be evident from the ultrasound image may be overlooked because they occur so rarely that an operator would lack sufficient experience to be able readily to recognise those abnormalities.

SUMMARY OF THE INVENTION

It is an object of the invention to improve the detection of medical abnormalities from non-invasively scanned images.

This invention provides a non-invasive medical scanning apparatus comprising: scanning means for non-invasively generating an image of at least an interior region of a subject to be examined; and means for detecting a quantitative measure indicative of the shape of said image, said quantitative measure having a correlation with the presence of a medical abnormality in said subject.

This invention addresses the problem that some rare medical abnormalities may be evident from a non-invasively scanned image of the patient, but the recognition by an operator of these abnormalities may

be difficult (through lack of operator experience) and time consuming.

As an example, the condition of spina bifida in a fetus is indicated by a deformation of the fetal head. This deformation (known as the "lemon" sign) shows up on an ultrasound scan of the fetus within the mother's uterus, but the fact that spina bifida occurs in only about one in one thousand term births means that (a) the scanning operator would have to, on average, examine 1000 ultrasound images to detect one case of spina bifida; and (b) many operators would only be likely to see one or two cases of spina bifida per year, and so would not develop the experience to be able to detect the deformation or abnormality.

The invention solves this problem by detecting a quantitative measure indicative of the shape of the non-invasively scanned image and correlated with the presence of a medical abnormality. This process can be performed automatically when each image is generated, and can be used (for example) to generate an alarm signal to prompt further medical investigations, such as more detailed scanning or further testing by an expert in that medical field.

The quantitative measure can be used in various ways in order to assist an operator to be made aware of the medical abnormality in question. For example, in one preferred embodiment, the apparatus comprises means for displaying a numerical value indicative of said quantitative measure. In another preferred embodiment, the apparatus comprises means for detecting whether said quantitative measure lies in a range indicative of possible presence of said medical abnormality.

In order to attract the operator's attention in the case of a detection of a possible medical abnormality, it is preferred that the apparatus comprises means for generating an alarm signal in response to a detection that said quantitative measure lies in said range indicative of said possible medical abnormality.

In a preferred embodiment the apparatus comprises an alphanumeric display; and in said alarm signal comprises an alarm message for display on said alphanumeric display.

Although the quantitative measure can be compared with static data representing an overall population, it is preferred that data derived from the scanned images can be archived, in order that future images may be compared with the archived data. Accordingly, in a

preferred embodiment, the apparatus comprises means for storing data relating to previous occurrences of said medical abnormality; and means for comparing said quantitative measure with said stored data relating to said previous occurrences of said medical abnormality. In particular, it is preferred that said stored data comprises data indicative of a statistical distribution of said quantitative measure in said previous occurrences of said medical abnormality.

In a preferred embodiment the apparatus comprises means for deriving a likelihood ratio from said detected quantitative measure and said stored data, said likelihood ratio indicating a relative likelihood of occurrence of said medical abnormality in a current subject. Preferably the apparatus also comprises means for displaying said likelihood ratio for said current subject.

The likelihood ratio may simply be displayed, for evaluation by the operator. However, it is preferred that the evaluation is performed at least in part automatically. To this end it is preferred that the apparatus comprises means for detecting whether said likelihood ratio lies in a predetermined range; and means for generating an alarm signal if said likelihood ratio lies in said predetermined range.

The likelihood ratio is preferably combined with the "prior risk" of the occurrence of the medical abnormality. To this end, it is preferred that the apparatus comprises input means for user input of a prior risk value, said prior risk value indicating a statistical occurrence of said medical abnormality; and means for deriving an absolute risk value by deriving a product of said prior risk value and said likelihood ratio. For example, if the prior risk is 1:1000 (1 case in 1000 population) and the likelihood ratio is 3, then the absolute risk value would be 3:1000.

Preferably the analysis of the scanned image is combined with analysis of other tests which can support a diagnosis of the abnormality in question. It is thus preferred that the apparatus comprises input means for input of test data indicative of a further test for said medical abnormality. It is also preferred that the apparatus comprises means for combining said test data with said quantitative measure and said stored data, to generate said likelihood ratio.

Although the further tests could take many forms, it is preferred that said test data is indicative of a result of a biochemical test performed on said subject.

The input means could be as simple as a data entry keyboard. However, to allow for the electronic transfer of test data from other apparatus, it is preferred that the input means comprises an electronic data interface.

The derivation of the likelihood ratio is subject to the effects of random noise in the quantitative measure and (if applicable) the other tests performed. These effects can be reduced by allowing for variable factors relating to the current subject. It is therefore preferred that the apparatus comprises user input means for user input of subject data specifying one or more physical attributes of said subject, said means for deriving said likelihood ratio being responsive to said subject data.

Preferably said subject data comprises at least one of:

(i) said subject's age; and

(ii) said subject's weight.

It is preferred that the apparatus comprises means for digitally enhancing said image. This may comprise means for high-pass spatially filtering said image. Means for detecting portions of said image having at least a predetermined luminance level may also be employed to detect portions of interest in the images. In order to detect edges within the images, it is preferred that the apparatus also comprises means for detecting portions of said image indicative of edges of said interior region of said subject, in conjunction with, preferably, means for detecting gaps in said edges; and means for filling said gaps in said edges, to provide a substantially continuous edge in said image.

The archiving of the eventual diagnosis of the presence or lack of the medical abnormality is facilitated by the use of input means for subsequent user input of data indicative of a later diagnosis of said medical abnormality in said subject.

In one preferred embodiment, said subject is a pregnant female; and said image is an image of a fetus. In this case, it is preferred that said biochemical test comprises one or more tests selected from the group consisting of:

(i) a detection of said subject's level of human chorionic

gonadotrophin;

(ii) a detection of said subject's level of alpha-feto protein;

(iii) a detection of said subject's level of unconjugated oestriol;

(iv) a detection of said subject's level of pregnancy associated placental protein-A (PAPP-A);

(v) a detection of said subject's level of the free alpha subunit of human chorionic gonadotrophin; and

(vi) a detection of said subject's level of the free beta subunit of human chorionic gonadotrophin.

In order to allow the detection of possible cases of, for example, spina bifida, it is preferred that said image comprises a sectional image of a fetal head; and said apparatus comprises means for detecting an outline of said image of said fetal head.

In another embodiment, to allow for the detection of possible cases of Down's syndrome, it is preferred that said image comprises a sectional image of the nuchal fold of said fetus; and said apparatus comprises means for detecting an outline of said image of said nuchal fold. Alternatively, the thickness of the nuchal fold could be examined, in which case it is preferred that said image comprises a sectional image of the nuchal fold of said fetus; and said apparatus comprises means for detecting a thickness of said image of said nuchal fold.

In the case of a pregnant subject, it is preferred that said subject data comprises data indicative of the gestational age of said fetus.

In another embodiment, a detection of possible cases of ovarian cancer can be made. To this end, it is preferred that said image comprises a sectional image of said subject's ovary; and said means for detecting a quantitative measure comprises means for detecting an outline of said image of said ovary.

Preferably said means for detecting a quantitative measure comprises means for detecting a length of at least one axis of said outline. More specifically, it is preferred that said means for detecting a quantitative measure is operable to generate a numerical value indicative of a ratio of lengths of axes of said outline.

A number (at least two) of quantitative measures may be detected

and the results combined using standard statistical techniques.

In respective preferred embodiments, the scanning means comprises means for generating an ultrasound (US) image of at least said interior region of said subject; means for generating a computer aided tomographic (CAT) image of at least said interior region of said subject; means for generating a single-photon emission computed tomographic (SPECT) image of at least said interior region of said subject; means for generating a positron emission tomographic (PET) image of at least said interior region of said subject; or means for generating a magnetic resonance (MRI) image of at least said interior region of said subject.

The invention may be embodied as a unit which is separate from, but works in conjunction with, a conventional ultrasound scanning device. To this end, in a second aspect this invention provides image processing apparatus for processing a non-invasively scanned image of at least an interior region of a subject, said apparatus comprising: means for detecting a quantitative measure indicative of the shape of said image, said quantitative measure having a correlation with the presence of a medical abnormality in said subject.

Viewed from a third aspect this invention provides a method of non-invasive medical scanning, said method comprising the steps of: non-invasively generating an image of at least an interior region of a subject to be examined; and detecting a quantitative measure indicative of the shape of said image, said quantitative measure having a correlation with the presence of a medical abnormality in said subject.

Viewed from a fourth aspect this invention provides a method of image processing a non-invasively scanned image of at least an interior region of a subject, said method comprising the steps of: detecting a quantitative measure indicative of the shape of said image, said quantitative measure having a correlation with the presence of a medical abnormality in said subject.

Viewed from a fifth aspect this invention provides a scanning method for identifying a medical abnormality comprising the steps of: non-invasively scanning an object internally of a body to produce image data corresponding to the object; processing the image data to generate at least one quantitative parameter corresponding to at least one physical characteristic of the object indicative of a medical

abnormality; generating a value as a function of the at least one quantitative parameter, wherein said value corresponds to a relationship between the at least one physical characteristic of the object and the at least one physical characteristic of an object not indicative of the medical abnormality; and determining a likelihood of the medical abnormality based upon the value.

Viewed from a sixth aspect this invention provides a method for identifying a medical abnormality comprising the steps of: receiving image data corresponding to a non-invasively scanned object internal of a body and processing the image data to generate at least one quantitative parameter corresponding to physical characteristics of the object indicative of a medical abnormality; generating a value as a function of the at least one quantitative parameter, wherein said value corresponds to a relationship between the at least one physical characteristic of the object and the at least one physical characteristic of an object not indicative of the medical abnormality; and determining a likelihood of the medical abnormality from the value.

Viewed from a seventh aspect this invention provides an apparatus for identifying a medical abnormality comprising: means receptive of image data corresponding to a non-invasively scanned object internal of a body for processing the image data to generate at least one quantitative parameter corresponding to physical characteristics of the object indicative of a medical abnormality; means for generating a value as a function of the at least one quantitative parameter, wherein said value corresponds to a relationship between the at least one physical characteristic of the object and the at least one physical characteristic of an object not indicative of the medical abnormality; and means receptive of the value for determining a likelihood of the medical abnormality.

Viewed from an eighth aspect this invention provides a scanning apparatus for identifying a medical abnormality comprising: means for non-invasively scanning an object internally of a body to produce image data corresponding to the object; means for processing the image data to generate at least one quantitative parameter corresponding to at least one physical characteristic of the object indicative of a medical abnormality; means for generating a value as a function of the at least one quantitative parameter, wherein said value corresponds to a

relationship between the at least one physical characteristic of the object and the at least one physical characteristic of an object not indicative of the medical abnormality; and means receptive of the value for determining a likelihood of the medical abnormality.

In other words, embodiments of the invention allow quantitative abnormality detection criteria relating to the scanned image of the region of interest to be derived and archived. These may contain indications of the medical abnormality in question, and by utilizing digital image enhancement, detection algorithms, and pattern recognition techniques to process the electronic signature signal train of the scanned ultrasound (or other) image, a correlation indication (or set of correlation coefficients) can be computed which maps or map the scanned image into the archived criteria. That is to say, a variable is computed that can be used to distinguish normal from abnormal by comparison with the archived criteria.

The archived quantitative criteria can be derived from scanned images developed using the applicable scanning technique (e.g. Ultrasound (US), Computerized Axial Tomography(CAT), Magnetic Resonance Imaging (MRI), etc.), which are associated with the abnormality of interest. The derivation of the archived quantitative criteria recognises the special image characteristics of the population having a positive diagnosis of the abnormality, as well as the image characteristics of an unaffected population. The archived quantitative criteria will be appropriate for contemporary patient image generation equipment, techniques, and for operator interface and the scanning technique utilised in patient studies. In the example of an ultrasound scanned image, quantitative criteria could include dimensional criteria (e.g. length, width, thickness, etc.), ratio information (e.g. ratio of length to width), form-factor information (e.g. perimeter to area), area information, volumetric information, and relative density (e.g. intensity) information. Criteria are developed directly from the outputs of the scanning equipment, or from the development of relationships incorporating these outputs, and in any case from populations with and without the abnormality in question.

The scanned image of the region of interest (e.g. body, or portion of body, fetus, or portion of fetus) which is being evaluated for possible indications of the low prevalence abnormality is such that

this image may contain evidence of the abnormality. That evidence may not be readily recognized by the scanning equipment operator because of the low prevalence of the abnormality, and the concomitant experience level. In embodiments of the invention the scanned image is automatically processed to emphasize the image characteristics which describe the abnormality, provide discrimination, and relate to the archived criteria. The automated processing of the scanned image reduces both the amount and skill level of the operator effort required, and by providing a reproducible representation, can reduce uncertainty and bias which may result from operator interpretation. In the case of an ultrasound scanned image, for example, the automated processing can include image enhancement processes followed by pattern recognition processes. The automatically processed data will contain scanned image information for the specific image of interest, the detected image describing the region being studied (e.g. body or portion of body, fetus or portion of fetus). The automatically processed data will then be used, in conjunction with a software computer program tailored to the scanner type (e.g. ultrasonic), the medical abnormality of medical interest, and the characteristic indications as scanned, to generate image specific descriptors. These image specific descriptors are compared with the archived quantitative criteria which are derived from populations with and without the abnormality.

The image specific descriptors can provide a discriminant or set of discriminants for characterising the detected image measurement(s). The descriptors can be combined computationally to generate one or more figures of merit, which constitute a signature indicative of scanned image characteristics pertinent to the abnormality of interest. The set of image specific descriptors, combined into one or more figures of merit unique to the detected image of interest can then be correlated with the archived quantitative criteria developed from populations with or without the abnormality in question.

Techniques and standards for presenting, characterising and analysing assay data taken in conjunction with defect detection and risk estimation studies are known (e.g. biochemical), and embodiments of the invention are responsive to and compatible with these techniques and standards. In other words, embodiments of the invention handle the

acquisition and processing of data to provide risk estimation, and can relate the ultrasound risk estimation to the biochemical techniques available for such estimations. In some embodiments, threshold or cut-off values can be established for variables indicative of abnormality related risk, or more formal quantitative risk estimates can be calculated using the affected and unaffected data base, statistical modelling, and computational package techniques currently applied, for example to biochemical risk estimation using assay results, and patient risk factor analysis.

The techniques and processes of embodiments of the invention are independent of a specific imaging technology with respect to the elements of detection and measurement, archiving of quantitative criteria describing a population exhibiting positive diagnosis, and correlation of the image specific descriptors with the archived criteria to provide a quantitative indication of that correlation, a risk estimate.

As an example, spina bifida, a neural tube defect, and a congenital abnormality of the central nervous system (CNS) has an average incidence of about one in a thousand term births, although geographic variation in the rate of incidence does exist. The use of contemporary high-resolution ultrasound equipment provides significant potential for the evaluation of the fetal neural axis in early stages of fetal development, but the identification and possible quantification of selected CNS abnormalities such as spina bifida in many cases require a thorough knowledge and current experience in neuro abnormality. As currently emphasised, the accuracy and reliability of ultrasound scanning techniques in identifying and predicting spina bifida depend on the relevant experience and training of the operator, the capabilities of the ultrasound scanning equipment and the scope of the evaluation, including the time dedicated to the patient. The sensitivity and predictive value of non-targeted initial ultrasound examinations is probably quite low in most circumstances. Targeted (subsequent) examinations conducted on 'at risk' patients probably have significantly greater predictive value. In all cases involving the detection of spina bifida using ultrasound scanning techniques, operator training and experience, and available examination time per patient are limiting factors.

Embodiments of the invention provide an automated ultrasound image processing system for detecting potential cases of spina bifida, by the recognition and quantification of either an abnormal configuration of the cerebellum that appears as a crescent with the concavity pointing anteriorly ('banana sign'), or frontal bossing ('lemon sign'), or a combination of the two.

In one embodiment, for example, for the detection of the so-called 'lemon sign', the ultrasound scanner generates a sectional image of a fetal head and provides the means for the detection of spina bifida by the processing of measurements taken from the cross-sectional image. The ultrasound scanner provides means for detecting the principal (e.g. major and minor) axes of the outline of a cross-section of the fetal head. In this context, the major axis corresponds to the occipital-frontal measurement and the minor axis corresponds to the biparietal diameter of the fetal head. Various measurements can then be made with respect to the principal axes. Preferably the principal axes are detected by detecting the longest bisector of the outline (this being the major axis) and then the longest axis at 90° to the major axis (this being the minor axis). Shape characterisation includes the identification of the principal axis of the fetal head scan by a maximising algorithm which detects the longest bisector of the fetal head outline, while the minor axis of the fetal head outline is detected as the longest axis at 90° to the major axis.

Various measurements can be used to detect the condition of spina bifida. In one preferred embodiment the apparatus comprises means for providing the signal enhancement and processing necessary to detect the width of the fetal head at a position of 80% of the major axis of the outline, and for computing a figure of merit or descriptor by dividing that width by the sum of the lengths of the major and minor axes. In another preferred embodiment the apparatus comprises means for providing the signal enhancement and processing necessary to detect the lengths of axes extending from the centre of the major axis at an angle (such as 40°) to the major axis, and for computing a figure of merit by dividing the sum of those lengths by the sum of the lengths of the major and minor axes.

BRIEF DESCRIPTION OF THE DRAWINGS

The invention will now be described by way of example with

reference to the accompanying drawings, throughout which like parts are referred to by like references, and in which:

Figure 1 is a schematic diagram of an ultrasound scanning and defect detection apparatus;

Figure 2 illustrates various cross-sectional planes through a fetal head;

Figure 3 represents an ultrasound scan of the head of a fetus not suffering from spina bifida;

Figure 4 represents the ultrasound scan of a fetus suffering from spina bifida;

Figures 5 and 6 are schematic diagrams showing measurements made with respect to the principal axis of a fetal head scan to detect possible fetal abnormalities;

Figure 7 is a schematic diagram illustrating the statistical distribution of a quantitative value derived from the shape of a fetal head outline;

Figure 8 illustrates the derivation of a likelihood ratio;

Figure 9 illustrates a risk management system;

Figures 10 to 13 illustrate patient management protocols; and

Figures 14 and 15 are schematic diagrams of two further embodiments of an outline detector for detecting an outline of a non-invasively scanned image.

DESCRIPTION OF THE PREFERRED EMBODIMENTS

Figure 1 is a block diagram of a defect detection system which is used as part of or in conjunction with an ultrasound scanner to detect a spina bifida abnormality. A central processor with keyboard entry 10 and a central processor memory 20 combine to provide the computational, data processing, transactional memory, and application program storage and execution capabilities and implementation functionality necessary to process digital image data, develop shape characterization descriptors or figures of merit for specific images of interest, perform correlation against quantitative archived criteria, and provide a quantitative risk or categorical indication in comparison with a specified cut-off level.

An ultrasound scanner 30 suitable for ultrasonography for obstetric and gynaecological use will provide image data for the body

or portion of a body, fetus or portion of a fetus of interest. In a preferred embodiment for the detection of fetal abnormalities, the image data will characterize the fetal skull, or more specifically, a cross section of a fetal skull. The ultrasound scanner 30 may provide the image data directly in digital form, or may require the use of a commercially available digital scan converter 40 to convert the ultrasound scanner analog image data to digital form, in the case of ultrasound scanners providing analog image data only.

A high frequency emphasis filter 50 is used to emphasize the skull (outline) portion of the image while suppressing any random noise or "clutter" in the image. The skull portion of the image comprises relatively narrow, sharp regions that contain higher spatial frequencies. In contrast, the background clutter tends to be broad, slowly changing areas of the image that contain lower spatial frequencies. The processing of the image with a high frequency emphasis digital filtering process before applying a grey level intensity threshold processor 60 can be used to further improve and isolate the skull image.

The generation of the skull outline from the isolated skull image is a two-step process requiring edge detection and gradient and zero crossing detector 70. First, the inner and outer edges of the skull image are sharpened by the use of a gradient operator. For example, the so-called "Robert's cross" operator is a four point gradient operator that generates the gradient at each pixel using the intensity of the pixel and three neighbouring pixels. The mid-point of each edge can be detected by applying the gradient detector a second time and identifying zero crossings.

The second stage of the outline process is carried out by a thinning and contour tracing processor 80. The thinning algorithm produces a single-pixel wide trace between the two skull edges. However, this trace may have small, spurious branches or voids that are artifacts from the original image. The spurious branches and artifacts are removed by an artifact processor 90 using contour tracing algorithms that detect the spurs by evaluating the neighbours of each pixel on the outline trace. Voids are filled by a smoothing processor 100 by interpolating between isolated segments along the outline. If the processing algorithms were not fully successful in removing

clutter, the interpolation process may confuse clutter artifacts with valid skull outline segments. The resultant skull outline can be superimposed onto the original image to allow the operator to evaluate the adequacy of the outline tracing process using a correction processor 110. If necessary, the operator can "help" the algorithms by designating which segments are skull and which are clutter using a cursor. The interpolation process can be rerun with this additional information to produce a satisfactory result.

A shape characterization processor 120 combines the processed measurements extracted from the image using the algorithms developed for that purpose. A correlation processor 130 compares the shape characterization descriptors (e.g. figure of merit) with the archived quantitative criteria which characterize the fetal abnormality of interest to develop a quantitative risk indication (e.g. estimate, relationship to threshold value).

A display 140 and archived memory 150 (to store data representing images from an overall population, which may represent previous images scanned by the present apparatus) are included in the system.

In each case, length, as used in computation of risk estimate, represents the image presented by the scanner, as enhanced and processed in accordance with detection augmentation algorithms. Detection algorithms are permanently programmed in the system software and associated processor.

Detection Algorithms:

a. Normal ray ratio.
b. Oblique ray ratio from BPD from centre.
c. Scallop detector.
d. Frontal radius evaluator.
e. Radius of curvature distribution.
f. Radius of curvature first derivative distribution.
g. Deviation from an ellipse.
h. Correlation with known good/bad outlines.
i. Asymmetry.

Various of the image processing techniques are described in the book "Fundamentals of Digital Image Processing" (A.K. Jain, Prentice-Hall International, 1989).

Figure 2, provided for purposes of illustration, indicates three common scanning planes used in ultrasonography of the fetal skull. The present embodiment uses a standard scanning procedure. The three scanning planes illustrated in Figure 2 are the so-called "lateral ventricles" plane, the so-called "bpd-hc" plane and the so called "cerebellum" plane.

Figure 3 represents an ultrasound scan 160 of the head of a fetus suffering from spina bifida. The scan represents a cross section through the fetal head in the bpd-hc plane illustrated in Figure 2.

Figure 4 represents a similar scan 180 of the head of a fetus not suffering from spina bifida. The significant differences between the scan 160 and the scan 180, which differences are indicative of the spina bifida abnormality, are the slight depressions 170 in the spina bifida scan. These depressions 170 give the head the characteristic "lemon" shape and so are known as the "lemon" sign.

In the present embodiment used to detect spina bifida, measurements of length are enhanced, processed, and used to compute ratios (e.g. figures of merit) which form a descriptor set for the fetal image of interest. This descriptor set is correlated with the archived quantitative criteria derived from a statistically valid population having a positive diagnosis of the abnormality, spina bifida.

In this preferred embodiment used for the detection of spina bifida, and also applicable in instances where precise, repeatable fetal skull cross sectional measurements must be developed from the "raw" (e.g. unprocessed) scanner signal stream, digital image enhancement and pattern recognition are employed. The system processor, and its associated software control these functions.

Figures 5 and 6 are schematic diagrams showing examples of measurements which may be made with respect to the principal axis or axes of the fetal head outline, which measurements may then be used by the correlation processor to detect a possible fetal abnormality. In Figures 5 and 6 the length of the major axis of the fetal head outline is denoted by "l", and the length of the minor axis of the fetal head outline is denoted by "h".

Referring to the annotations on Figure 5, a variable n representing the shape of the fetal head outline is calculated as

follows:

$$n = \frac{d_1 + d_2}{l + h}$$

In the case of Figure 6, a similar variable m representing the fetal head shape is calculated as follows:

$$m(\theta) = \frac{s_1 + s_2}{l + h}$$

The variable n and m are examples of descriptors, or figures of merit. They may simply be displayed on a display means, compared with various numerical ranges as described below, or used to calculate a likelihood ratio or absolute risk (see below).

A thresholding or cut-off technique may be used to indicate a potential abnormality. In this case, the shape detector compares (correlates) the numerical value (descriptor) of the variables n or m with a cut-off (threshold) value. If the necessary value is below or above (as appropriate) the cut-off value, an alarm indication (e.g. a light, a sounder or an alphanumeric message on a display) can be automatically generated. The cut-off value is selected to reflect a balance between the detection of the greatest possible of possible instances of spina bifida (maximising the detection rate) against the need to avoid an excessive false positive rate. Cut-off values determined in trials of the embodiment are listed below:

Variable (Descriptor)	Cut-Off Value	Detection Rate %	False Positive Rate
$\frac{d_1 + d_2}{1 + h}$	<0.275	32(23/71)	0(0/20)
	<0.290	55(39/71)	10(2/20)
$\frac{s_1 + s_2 \ (0=35°)}{1 + h}$	<0.458	65(46/71)	0(0/20)
	<0.466	78(55/71)	10(2/20)
$\frac{s_1 + s_2 \ (0=40°)}{1 + h}$	<0.445	59(42/71)	0(0/20)
	<0.448	68(48/71)	10(2/20)

The automated generation of the skull outline from the scanner image can reduce the amount and skill level of the labour required while producing a more faithful representation of the skull outline by reducing the uncertainty and bias that results from an operator drawn outline. These automated processes consist of image enhancement processes followed by the pattern recognition processes.

While digital processing of a single image does not increase the actual information content of the image, it facilitates the pattern recognition process by increasing the image contrast and reducing noise and clutter. Because of the sharp differential in the relative propagation velocities of sound through bone and tissue, the skull portion of the fetal image tends to be higher intensity than the other (tissue) areas of the image. This characteristic allows the application of a pixel intensity threshold process to the digitized image to delete clutter while retaining the skull data.

A second characteristic of the skull image permits the use of high frequency emphasis filtering to emphasize the skull portion of image while suppressing the clutter in the image. The skull portion of the image consists of relatively narrow, sharp regions that contain higher spatial frequencies. The background clutter tends to be broad, slowly changing areas of the image that contain lower spatial frequencies. The processing of the image with a high frequency emphasis digital filtering process before applying the intensity threshold process is used to further improve and isolate the skull image.

The generation of the skull outline from the isolated skull image is a two step process. First, the inner and outer edges of the skull image are sharpened by the use of a gradient operator. The Robert's cross operator is a four point gradient operator that generates the gradient at each pixel using the intensity of the pixel and three of its neighbours. The mid-point of each edge if detected by applying the gradient detector a second time and identifying zero crossings.

The second stage of the outline process is a thinning and contour tracing process. The thinning algorithm produces a single-pixel wide trace between the two skull edges. However, this trace may have small, spurious branches or voids that are artifacts from the original image. The spurious branches are removed using contour tracing algorithms that

detect the spurs by evaluating the neighbours of each pixel on the outline trace. Voids are filled by interpolating between isolated segments along the outline. If the processing algorithms were not fully successful in removing clutter, the interpolation process may confuse clutter artifacts with valid skull outline segments. The resultant skull outline can be superimposed onto the original image to allow the operator to evaluate the adequacy of the outline tracing process. If necessary, the operator can "help" the algorithms by designating which segments are skull and which are clutter using a cursor. The interpolation process can be rerun with this additional information to produce an optimized result.

Preferably the results of two separate ultrasonography tests are combined, in order to increase the reliability of the detection of the possible medical abnormality. To this end it is preferred that the embodiment detects at least two quantitative measures relating to the image; and that the variable (descriptor) indicative of the shape of the image is detected in response to the at least two detected quantitative measures. Increased dimensionality of the correlation, and higher orders of discrimination will be provided where required by detection strategy.

In this embodiment, and in order that an operator is alerted to the detection of a possible medical abnormality and can then (if appropriate) initiate further testing or investigation of the patient, it is preferred that the embodiment comprises means for automatically generating an alarm indication in response to a detection that the variable (descriptor variable) lies in the range indicative of a possible medical abnormality (e.g below the thresholds described above).

This is one of a range of possible strategies for conducting, intervening, utilizing, and reporting on data presented by the embodiment. Other strategies will now be discussed.

The alarm indication could take the form of, for example, an audible warning or the illumination of an indicator light on an operator's console. In an alternative embodiment an alphanumeric display is used for use alone or in combination with other indicators of the condition under investigation, to display an appropriate alarm message.

The acquisition, processing, and archiving of ultrasound defect detection data, and the development of risk estimates will be consistent with the techniques and standards employed in risk estimation programs (e.g. biochemical).

Another embodiment allows for the detection of potential cases of Down's syndrome. The overall birth prevalence of Down's syndrome (trisomy 21) is about 1.3 in 1000 births, and is the most common cause of severe mental retardation in humans. Performing a fetal karyotype is the definitive method of diagnosis, and biochemical assays can be used in combination to identify a high risk group and provide for individual pregnancies. While many of the structural abnormalities associated with Down's syndrome are too subtle to be detected with current ultrasound equipment, several morphologic signs have been identified which indicate an elevated risk of Down's syndrome, and which can be detected by contemporary ultrasound techniques. These include a thickened nuchal fold, shortened femurs, and hypoplasia of the middle phalanx of the fifth digit.

A modified transverse view of the fetal head, including the cerebellum and occipital bone is used to detect abnormal thickening of the soft tissues at the back of the fetal occipital. The nuchal fold is usually measured from the outer edge of occipital bone to the outer edge of the fetal skin. As in the case of spina bifida, this embodiment provides the automatic signal processing, image enhancement, and pattern recognition to detect potential cases of Down's syndrome risk, as indicated by a thickened nuchal fold. In other words, the outline or thickness of the nuchal fold is detected.

Fetuses exhibiting Down's syndrome tend to have somewhat shortened femur lengths, compared to an unaffected population. The femur length:biparietal diameter (BPD) ratio test also tends to be reduced compared to unaffected populations. The techniques and implementation provided by the spina bifida embodiment described above can be used to interpret femur length and the ratio of femur length to BPD.

In the detection of ovarian cancer (or carcinoma of the ovary, CaO), the use of transvaginal sonography provides a method of screening for ovarian cancer. Ovarian cancer, which constitutes a significant proportion of all gynaecological malignancies, and which has a poor 5

year survival rate, is often first detected in an advanced stage. The detection of ovarian cancer in an earlier stage may improve the prognosis. A further embodiment relating to transvaginal ultrasound images of the ovaries, will refine the capability of diagnostic techniques to recognize, for example, relatively enlargement of the ovary or abnormality in shape and morphological pattern.

The embodiment for the detection of ovarian cancer related abnormalities employs intensity (density), volumetric and dimensional (shape), and computed mass and mass differential descriptors and discriminants.

Figure 7 is a schematic diagram illustrating the relative distribution of exemplary populations affected and unaffected by a medical abnormality. In particular, Figure 7 is used here to illustrate the methodology be which risk estimates (e.g. likelihood) that a given condition, such as a fetal defect, are calculated. The methodology applies to the ultrasound spina bifida detection technique, to biochemical marker tests, and to the application of the present techniques to ultrasound and other imaging techniques which examine the body and portions of the body, the fetus, and portions of the fetus for indications of risk presented by other abnormal conditions. Figure 7 shows the relative frequency distributions of a variable (e.g. n, m) among an affected 510 and unaffected population 500, and is plotted in the instance in multiples of the median for the unaffected population. This illustrative example is derived from gestational age corrected maternal serum alpha-fetoprotein data for open spina bifida. the presentation, treatment, and statistical techniques used for this biochemical marker are well described and are typical of the methodology employed in the computation of likelihood estimates (risk). The derivations can allow for the influence of such factors as gestational age, maternal age, maternal weight, race, geographic residence, and insulin dependent diabetes.

The application of population statistics for a fetal defect of interest, and the calculation of likelihood ratios utilize well established statistical techniques. The embodiments incorporates these established statistical and computational techniques. The embodiments may also include the incorporation of features responsive to clinical practice requirements, patient safety, and Food and Drug

Administration, and/or European Community criteria.

The apparatus can receive patient-related data, such as the patient's age or weight, or the gestational age of a fetus, to reduce the effects of random noise on the distributions. Generally this will narrow each of the two distributions shown in Figure 7.

Figure 8 illustrates the calculation of a likelihood ratio. Given the statistical distributions illustrated in Figure 7, the likelihood ratio for a sample 505 is the ratio of the heights of the two relative distribution curves at that point, i.e. f2/f1. The likelihood ratio represents how much more likely that subject is to have the abnormality than a general member of the population, and so can be converted to an absolute risk of the abnormality by multiplying the likelihood ratio by the "prior risk" exhibited by the whole population. The likelihood ratio and absolute risks can be displayed, thresholded or used to trigger alarms as described above. The two curves shown in Figures 7 and 8 can simply be stored in the memory 150 by storing their means and standard deviations. If more variables are being considered, correlation coefficients between the variables should also be stored.

Alternatively, if a thresholding technique is used, the overlap of the two distributions means that a proportion of the affected population 500 will fall below the threshold and a proportion of the unaffected population 510 will fall above the threshold. These proportions constitute false negative results and false positive results. In order to reduce these false positives and negatives, additional factors such as the maternal weight may be considered to adjust the threshold values.

Figure 9 is a schematic diagram illustrating a further embodiment which recognises the common nature of much of the analytical and computational treatments of ultrasound and biochemical risk estimation data. The principles of risk estimation based on univariate and multivariate (e.g Gaussian) distributions are common to the ultrasound defect detection, and the more mature, biochemical testing and fetal defect risk estimation techniques.

Biochemical risk estimation using the results of assays involving two or more markers is performed by the application of software computer programs to interpret results. These programs take account of

disease prevalence distributions of the markers and their correlation, and other factors that may be relevant such as gestational age and maternal weight. Ultrasound defect detection and risk estimation use these automated computer techniques, as well as the image associated techniques described in this disclosure. In both the biochemical case and the ultrasound case, "raw" (unprocessed) data will be available either on a "real time" basis, using an "RS 232" or other standard communications protocol, or on a delayed time basis (days, weeks), by data entry.

Figure 9 illustrates a risk management system having computational elements (e.g. a central processor unit 610, a memory 620, an input-output processor 630, and a local/wide area communication network 640) which meet the requirements of both ultrasound and biochemical derived risk estimation methodologies are consistent and compatible. The risk management system 600 provides the functional means of implementing both ultrasound and biochemical risk estimation using data sources now available. This embodiment integrates the elements of ultrasound detection with biochemical and patient data in a single, integrated risk management central processing unit.

Figure 10 illustrates a decision making protocol which incorporates data derived by biochemical and ultrasound techniques to detect congenital abnormalities in the developing fetus. A level 1 ultrasound scanned image, using standard obstetric/gynaecological ultrasound equipment, augmented by the defect detection processor 300 (according to an embodiment of the invention) is used for dating (e.g., the assessment of gestational age), detection of possible fetal abnormalities as described in this disclosure (e.g., spina bifida, Down's syndrome), and for any other examinations requested by the physician and/or the laboratory. The estimation of gestational age resulting from the ultrasound examination utilizes standard techniques and will be derived from measurements appropriate to the specific circumstances (e.g. reliability, ease of measurement). Measurements may include crown-rump length (CRL) or biparietal diameter (BPD) for assessment of gestational age. The estimated gestational age resulting from this dating measurement can improve the performance of biochemical screening since the biochemical marker measurements are influenced by gestational age.

The data derived from the ultrasound image augmented by the present embodiments will provide an indication of fetal abnormalities by processing and enhancing measurement data, calculating descriptor variables (e.g., n and m), and relating the variable value(s) to criteria (e.g., cut-off values). The results of the defect detection process will be available at a time in the gestational cycle which is influenced by the age assessment technique, and the specific ultrasound abnormality detection technique. Abnormality detection using ultrasound techniques can be accomplished relatively early in the gestational cycle, allowing directed follow-up and biochemical testing where results indicate a fetal abnormality.

Maternal serum biochemical testing 310 is based on the measurement of such marker levels as alphafetoprotein (AFP), human chorionic gonadotrophin (hCG), unconjugated oestriol (uE3), pregnancy associated placental protein A (PAPP-A), free alpha subunit of human chorionic gonadotrophin (alpha hCG), and free beta subunit of human chorionic gonadotrophin (beta hCG) (from a pregnant patient in a specified gestational range) in maternal serum. Risk estimation required integration of the individual marker levels, using appropriate statistical methods. In general the results are influenced by estimated gestational age, so that more effective ultrasound dating increases the reliability of the risk estimate. The present embodiments allow the ultrasound markers (e.g. m, n) to be combined with the biochemical tests to improve the performance of screening.

Should maternal serum biochemical testing indicate abnormal results, testing a second specimen 320 may be carried out but is not normally recommended.

Should the biochemical testing of a second specimen of maternal serum indicate abnormal results level 2 ultrasound 330, high resolution (augmented by apparatus according to an embodiment of the invention), such as the defect detection processor described hereinbefore, will be performed. The level 2 ultrasound examination 330 will provide refined gestational age assessment, fetal abnormality detection as provided by these embodiments and provision for expanded scope and/or directed follow-up. Abnormal results from the multi-stage screening approach indicate the need for amniotic fluid testing, fetal karyotyping and a more detailed diagnostic ultrasound examination.

Amniotic fluid biochemical testing 340 is similar to maternal serum biochemical testing 310 in its use of measured marker levels, interpretation in relation to specified cut-off levels, integrated statistical processing of individual marker results, and calculation of risk estimates for defects of interest. Amniotic fluid tests include alpha-fetoprotein and acetylcholinesterase measurement and fetal karyotyping. Detailed ultrasonography is also carried out. Appropriate follow-up includes patient counselling.

The present embodiments can thus provide a means for augmenting an accepted protocol recommended (e.g. by the United States Food and Drug Administration) for use in decision making by and counselling for patients undergoing testing for fetal abnormalities. This protocol, outlined in Figure 9, does not include the automatic defect detection capabilities provided here. The sequence of the protocol steps, and the criteria for both need and timing in the gestational cycle are modified to improve the performance of screening for fetal defects.

In contrast, in the standard protocol illustrated in Figure 11, the maternal biochemical serum testing 400 is identical to the maternal serum biochemical testing 310 described in Figure 10. The second specimen maternal serum biochemical testing 410 is identical to the second specimen testing 320 shown in Figure 10. The biochemical amniotic fluid testing 430, is identical to the amniotic fluid biochemical testing 340 shown in Figure 10. Confirmatory tests 350 are similar to these indicated 440 in Figure 10. In the modified protocol shown in Figure 10, all ultrasound testing 300, 330, and 350, include defect detection capability resulting from the augmentation of the standard ultrasound scanner by these embodiments.

Protocol step 330, the early augmented ultrasound scanning test incorporating an embodiment of the present invention, is introduced formally into the recommended protocol to provide the benefits of early defect detection with respect to treatment, additional testing, decision making and patient counselling. The embodiments thus influence the decisions and the timing of subsequent protocol phases. All protocol steps in Figure 10 involving ultrasound scanning; 300, 330, and 350 include the augmentation provided by the embodiments, the automatic defect detection capability.

In the standard protocol, Figure 11, protocol steps involving

ultrasound scanning, 420 and 440, utilize standard ultrasound scanning technique, and do not provide automatic defect detection capability. The standard protocol does not provide the flexibility and timing benefits of the step 1 augmented ultrasound test 300 indicated in Figure 10.

Figures 12 and 13 are schematic illustrations of two further decision making protocols incorporating apparatus according to the present embodiments. In Figure 12, an initial blood test and a level 1 ultrasound (as described above) are carried out in parallel, and in Figure 13 they are carried out sequentially. A positive indication in either case leads to more detailed testing. In either case, whether the pregnancy leads to birth or termination, the actual outcome (i.e. the actual presence of the abnormality) is stored in the memory 150 along with the quantitative descriptors derived from images of that patient. These values can be used to modify the population distributions of Figure 7, to tend to increase the accuracy of future diagnoses.

Figures 14 and 15 are schematic diagrams of two further embodiments of an outline detector for detecting an outline of a non-invasively scanned image. In each of Figures 14 and 15, the image outline is indicated by the user tracing the outline on the screen of a video display device 970. In the embodiment shown in Figure 14, the user employs a light pen 980, connected to an image processor 950 and a video memory 960 storing the image data, to trace the image outline, whereas in Figure 15 the user employs a mouse-or key-driven cursor generated by an image processor 990 to trace the image outline.

The embodiments provide a positive means for modifying the generally accepted decision making protocol for prenatal detection of Down's syndrome and neural tube defects to provide benefits of timing, flexibility, and opportunity for treatment and additional early testing.

Although illustrative embodiments of the invention have been described in detail herein with reference to the accompanying drawings, it is to be understood that the invention is not limited to those precise embodiments, and that various changes and modifications can be effected therein by one skilled in the art without departing from the scope and spirit of the invention as defined by the appended claims.

CLAIMS

1. Non-invasive medical scanning apparatus comprising:

scanning means for non-invasively generating an image of at least an interior region of a subject to be examined; and

means for detecting a quantitative measure indicative of the shape of said image, said quantitative measure having a correlation with the presence of a medical abnormality in said subject.

2. Apparatus according to claim 1, comprising means for displaying a numerical value indicative of said quantitative measure.

3. Apparatus according to claim 1 or claim 2, comprising means for detecting whether said quantitative measure lies in a range indicative of possible presence of said medical abnormality.

4. Apparatus according to any one of the preceding claims, comprising means for generating an alarm signal in response to a detection that said quantitative measure lies in said range indicative of said possible medical abnormality.

5. Apparatus according to claim 4, comprising: an alphanumeric display; and in which said alarm signal comprises an alarm message for display on said alphanumeric display.

6. Apparatus according to any one of the preceding claims, comprising:

means for storing data relating to previous occurrences of said medical abnormality; and

means for comparing said quantitative measure with said stored data relating to said previous occurrences of said medical abnormality.

7. Apparatus according to claim 6, in which said stored data comprises data indicative of a statistical distribution of said quantitative measure in said previous occurrences of said medical abnormality.

8. Apparatus according to claim 6 or claim 7, comprising means for deriving a likelihood ratio from said detected quantitative measure and said stored data, said likelihood ratio indicating a relative likelihood of occurrence of said medical abnormality in a current subject.

9. Apparatus according to claim 8, comprising means for displaying said likelihood ratio for said current subject.

10. Apparatus according to claim 8 or claim 9, comprising:

means for detecting whether said likelihood ratio lies in a predetermined range; and

means for generating an alarm signal if said likelihood ratio lies in said predetermined range.

11. Apparatus according to any one of claims 8 to 10, comprising:

input means for user input of a prior risk value, said prior risk value indicating a statistical occurrence of said medical abnormality; and

means for deriving an absolute risk value by deriving a product of said prior risk value and said likelihood ratio.

12. Apparatus according to any one of the preceding claims, comprising: input means for input of test data indicative of a further test for said medical abnormality.

13. Apparatus according to claim 12 and any one of claims 9 to 11, comprising:

means for combining said test data with said quantitative measure and said stored data, to generate said likelihood ratio.

14. Apparatus according to claim 12 or claim 13, in which said test data is indicative of a result of a biochemical test performed on said subject.

15. Apparatus according to any one of claims 12 to 14, in which said input means comprises an electronic data interface.

16. Apparatus according to any one of claims 8 to 11, comprising:

user input means for user input of subject data specifying one or more physical attributes of said subject, said means for deriving said likelihood ratio being responsive to said subject data.

17. Apparatus according to claim 16, in which said subject data comprises at least one of:

(i) said subject's age; and

(ii) said subject's weight.

18. Apparatus according to any one of the preceding claims, comprising means for digitally enhancing said image.

19. Apparatus according to claim 18, in which said means for digitally enhancing said image comprises means for high-pass spatially filtering said image.

20. Apparatus according to claim 18 or claim 19, comprising means for detecting portions of said image having at least a predetermined luminance level.

21. Apparatus according to any one of claims 18 to 20, comprising means for detecting portions of said image indicative of edges of said interior region of said subject.

22. Apparatus according to claim 21, comprising:

means for detecting gaps in said edges; and

means for filling said gaps in said edges, to provide a substantially continuous edge in said image.

23. Apparatus according to any one of the preceding claims, comprising input means for subsequent user input of data indicative of a later diagnosis of said medical abnormality in said subject.

24. Apparatus according to any one of the preceding claims, in which:

said subject is a pregnant female; and

said image is an image of a fetus.

25. Apparatus according to claim 14 and claim 24, in which said biochemical test comprises one or more tests selected from the group consisting of:

(i) a detection of said subject's level of human chorionic gonadotrophin;

(ii) a detection of said subject's level of alpha-fetoprotein;

(iii) a detection of said subject's level of unconjugated oestriol;

(iv) a detection of said subject's level of pregnancy associated placental protein-A (PAPP-A);

(v) a detection of said subject's level of the free alpha subunit of human chorionic gonadotrophin; and

(vi) a detection of said subject's level of the free beta subunit of human chorionic gonadotrophin.

26. Apparatus according to claim 24 or claim 25, in which:

said image comprises a sectional image of a fetal head; and

said apparatus comprises means for detecting an outline of said image of said fetal head.

27. Apparatus according to claim 24 or claim 25, in which:

said image comprises a sectional image of the nuchal fold of said fetus; and

said apparatus comprises means for detecting an outline of said image of said nuchal fold.

28. Apparatus according to claim 24 or claim 25, in which:

said image comprises a sectional image of the nuchal fold of said fetus; and

said apparatus comprises means for detecting a thickness of said image of said nuchal fold.

29. Apparatus according to any one of claims 24 to 28, in which said subject data comprises data indicative of the gestational age of said fetus.

30. Apparatus according to any one of claims 1 to 23, in which:

said image comprises a sectional image of said subject's ovary; and

said means for detecting a quantitative measure comprises means for detecting an outline of said image of said ovary.

31. Apparatus according to any one of claims 23, 24, 25, 26, 28, 29 and 30, in which said means for detecting a quantitative measure comprises means for detecting a length of at least one axis of said outline.

32. Apparatus according to claim 31, in which said means for detecting a quantitative measure is operable to generate a numerical value indicative of a ratio of lengths of axes of said outline.

33. Apparatus according to any one of the preceding claims, comprising:

means for detecting at least two quantitative measures relating to said image.

34. Apparatus according to any one of the preceding claims, in which said scanning means comprises means for generating an ultrasound image of at least said interior region of said subject.

35. Apparatus according to any one of claims 1 to 33, in which said scanning means comprises means for generating a computer aided tomographic image of at least said interior region of said subject.

36. Apparatus according to any one of claims 1 to 33, in which said scanning means comprises means for generating a single-photon emission computed tomographic image of at least said interior region of said subject.

37. Apparatus according to any one of claims 1 to 33, in which said scanning means comprises means for generating a positron emission tomographic image of at least said interior region of said subject.

38. Apparatus according to any one of claims 1 to 33, in which said scanning means comprises means for generating a magnetic resonance image of at least said interior region of said subject.

39. Image processing apparatus for processing a non-invasively scanned image of at least an interior region of a subject, said apparatus comprising:

means for detecting a quantitative measure indicative of the shape of said image, said quantitative measure having a correlation with the presence of a medical abnormality in said subject.

40. A method of non-invasive medical scanning, said method comprising the steps of:

non-invasively generating an image of at least an interior region of a subject to be examined; and

detecting a quantitative measure indicative of the shape of said image, said quantitative measure having a correlation with the presence of a medical abnormality in said subject.

41. A method of image processing a non-invasively scanned image of at least an interior region of a subject, said method comprising the steps of:

detecting a quantitative measure indicative of the shape of said image, said quantitative measure having a correlation with the presence of a medical abnormality in said subject.

42. An apparatus for identifying a medical abnormality comprising:

means receptive of image data corresponding to a non-invasively scanned object internal of a body for processing the image data to generate at least one quantitative parameter corresponding to physical characteristics of the object indicative of a medical abnormality;

means for generating a value as a function of the at least one quantitative parameter, wherein said value corresponds to a relationship between the at least one physical characteristic of the object and the at least one physical characteristic of an object not indicative of the medical abnormality; and

means receptive of the value for determining a likelihood of the

medical abnormality.

43. The apparatus according to claim 42, wherein the means for determining the likelihood of the medical abnormality comprises means for comparing the value to a predetermined cut-off value.

44. The apparatus according to claim 43, wherein the means for determining the likelihood of the medical abnormality comprises means receptive of data relating to the body and means for adjusting the predetermined cut-off value as a function of the data relating to the body.

45. The apparatus according to claim 44, wherein the data relating to the body is at least one of age and weight.

46. The apparatus according to claim 43, wherein the means for determining the likelihood of the medical abnormality comprises means receptive of biochemical data relating to the body or the object and means for adjusting the predetermined cut-off value as a function of the biochemical data.

47. The apparatus according to claim 46, wherein the biochemical data is at least one marker selected from the group consisting of human chorionic gonadotrophin, alpha-feto protein, unconjugated oestriol, placental protein A, free alpha human chorionic gonadotrophin, and free beta human chorionic gonadotrophin.

48. The apparatus according to claim 42, for identifying spina bifida in a fetus, wherein the object is a fetal skull and the at least one physical characteristic comprises a shape of an outline of the skull.

49. The apparatus according to claim 48, wherein the at least one quantitative parameter includes a length of a major and minor axis of the skull outline and a length of a chord situated at a given position along the major axis.

50. The apparatus according to claim 48, wherein the at least one

quantitative parameter includes a length of a major and minor axis of the skull outline and a length of radii situated at a given angle from the major axis.

51. The apparatus according to claim 48, wherein the means for processing the image data comprises means receptive of image data corresponding to the skull cross section for generating image data corresponding to the outline of the fetal skull and means for determining distances between preselected points on and within the outline.

52. The apparatus according to claim 42, for identifying down syndrome in a fetus, wherein the object is a fetal nuchal fold and the at least one physical characteristic is a shape of the nuchal fold, wherein the at least one quantitative parameters comprises a thickness of the nuchal fold.

53. The apparatus according to claim 42, for identifying ovarian cancer, wherein the object is an ovary and the at least one physical characteristic is the shape of the ovary.

54. The apparatus according to claim 42, further comprising means indicating a likelihood of the medical abnormality.

55. The apparatus according to claim 54, wherein the means indicating a likelihood of the medical abnormality includes means for generating an alarm signal when a likelihood greater than a preselected percentage is obtained.

56. The apparatus according to claim 55, wherein the means for generating an alarm signal comprises a display and means for generating an alarm message on the display.

57. A scanning apparatus for identifying a medical abnormality comprising:

means for non-invasively scanning an object internally of a body to produce image data corresponding to the object;

means for processing the image data to generate at least one quantitative parameter corresponding to at least one physical characteristic of the object indicative of a medical abnormality;

means for generating a value as a function of the at least one quantitative parameter, wherein said value corresponds to a relationship between the at least one physical characteristic of the object and the at least one physical characteristic of an object not indicative of the medical abnormality; and

means receptive of the value for determining a likelihood of the medical abnormality.

58. The scanning apparatus according to claim 57, wherein the means for processing the image data comprises means receptive of image data corresponding to a cross section of the object for generating image data corresponding to an outline of the object and means for determining distances between preselected points on and within the outline.

59. The scanning apparatus according to claim 57, wherein the means for scanning comprises an ultrasonic scanner.

60. An method for identifying a medical abnormality comprising the steps of:

receiving image data corresponding to a non-invasively scanned object internal of a body and processing the image data to generate at least one quantitative parameter corresponding to physical characteristics of the object indicative of a medical abnormality;

generating a value as a function of the at least one quantitative parameter, wherein said value corresponds to a relationship between the at least one physical characteristic of the object and the at least one physical characteristic of an object not indicative of the medical abnormality; and

determining a likelihood of the medical abnormality from the value.

61. The method according to claim 60, wherein the step of determining the likelihood of the medical abnormality comprises comparing the value

to a predetermined cut-off value.

62. The method according to claim 61, wherein the step of determining the likelihood of the medical abnormality comprises receiving data relating to the body and adjusting the predetermined cut-off value as a function of the data relating to the body.

63. The method according to claim 62, wherein the data relating to the body is at least one of age and weight.

64. The method according to claim 61, wherein the step of determining the likelihood of the medical abnormality comprises receiving biochemical data relating to the body or the object and adjusting the predetermined cut-off value as a function of the biochemical data.

65. The method according to claim 64, wherein the biochemical data is at least one marker selected from the group consisting of human chorionic gonadotrophin, alpha-feto protein, unconjugated oestriol, placental protein A, free alpha human chorionic gonadotrophin, and free beta human chorionic gonadotrophin.

66. The method according to claim 60, for identifying spina bifida in a fetus, wherein the object is a fetal skull and the at least one physical characteristic comprises a shape of an outline of the skull.

67. The method according to claim 66, wherein the at least one quantitative parameter includes a length of a major and minor axis of the skull outline and a length of a chord situated at a given position along the major axis.

68. The method according to claim 66, wherein the at least one quantitative parameter includes a length of a major and minor axis of the skull outline and a length of radii situated at a given angle from the major axis.

69. The method according to claim 66, wherein the step of processing the image data comprises receiving image data corresponding to the

skull cross section for generating image data corresponding to the outline of the fetal skull and determining distances between preselected points on and within the outline.

70. The method according to claim 60, for identifying down syndrome in a fetus, wherein the object is a fetal nuchal fold and the at least one physical characteristic is a shape of the nuchal fold, wherein the at least one quantitative parameters comprises a thickness of the nuchal fold.

71. The method according to claim 60, for identifying ovarian cancer, wherein the object is an ovary and the at least one physical characteristic is the shape of the ovary.

72. The method according to claim 60, further comprising indicating a likelihood of the medical abnormality.

73. The method according to claim 72, wherein the step of indicating a likelihood of the medical abnormality includes generating an alarm signal when a likelihood greater than a preselected percentage is obtained.

74. The method according to claim 73, wherein the step of generating an alarm signal comprises generating an alarm message on a display.

75. A scanning method for identifying a medical abnormality comprising the steps of:

non-invasively scanning an object internally of a body to produce image data corresponding to the object;

processing the image data to generate at least one quantitative parameter corresponding to at least one physical characteristic of the object indicative of a medical abnormality;

generating a value as a function of the at least one quantitative parameter, wherein said value corresponds to a relationship between the at least one physical characteristic of the object and the at least one physical characteristic of an object not indicative of the medical abnormality; and

determining a likelihood of the medical abnormality based upon the value.

76. The scanning method according to claim 75, wherein the step of processing the image data comprises receiving image data corresponding to a cross section of the object, generating image data corresponding to an outline of the object and determining distances between preselected points on and within the outline.

77. The scanning method according to claim 75, wherein the step of scanning comprises an ultrasonic scanning.

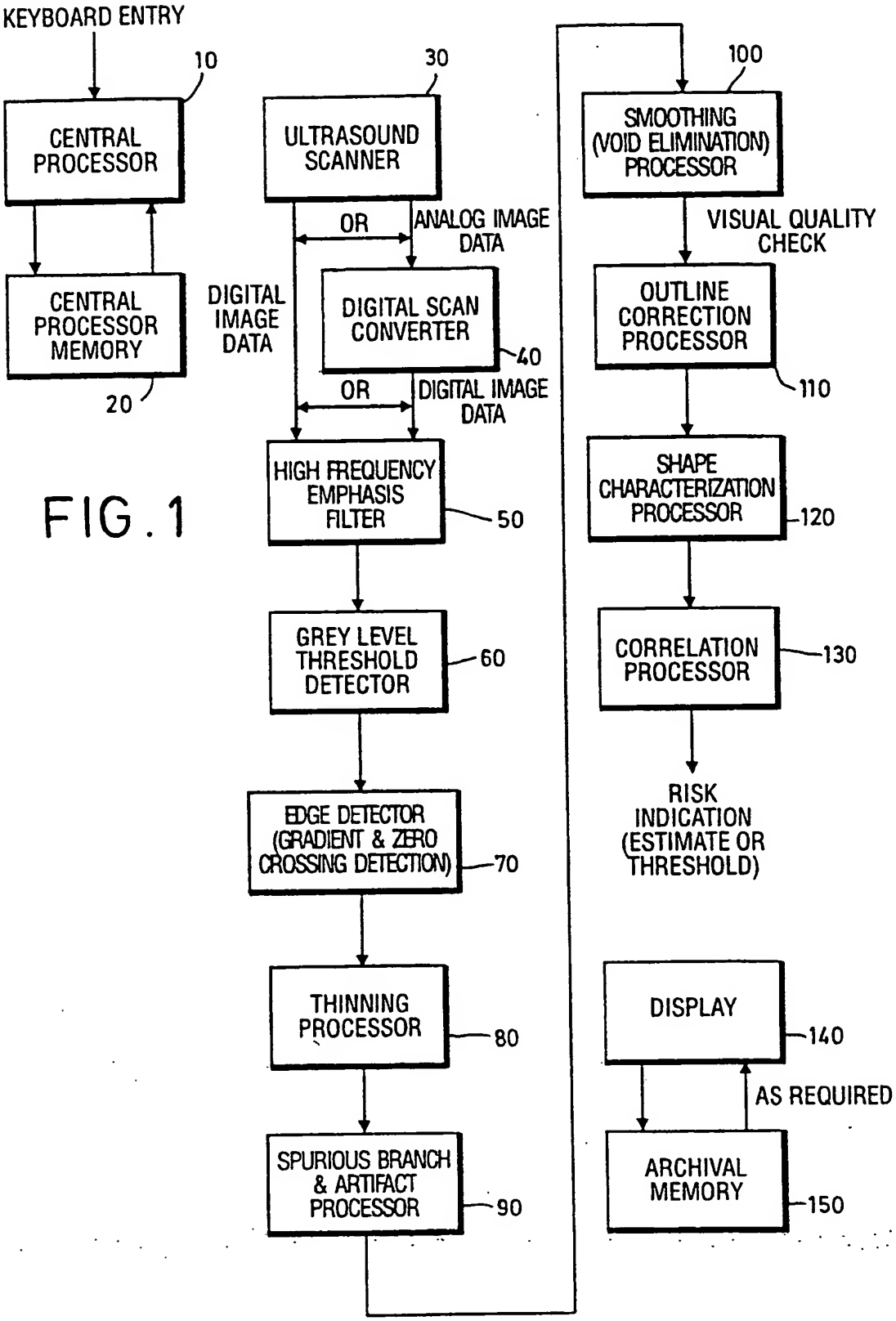

KEYBOARD ENTRY
10
CENTRAL PROCESSOR
CENTRAL PROCESSOR MEMORY
20
30
ULTRASOUND SCANNER
OR
ANALOG IMAGE DATA
DIGITAL IMAGE DATA
DIGITAL SCAN CONVERTER
40
OR
DIGITAL IMAGE DATA
HIGH FREQUENCY EMPHASIS FILTER
50
GREY LEVEL THRESHOLD DETECTOR
60
EDGE DETECTOR (GRADIENT & ZERO CROSSING DETECTION)
70
THINNING PROCESSOR
80
SPURIOUS BRANCH & ARTIFACT PROCESSOR
90
100
SMOOTHING (VOID ELIMINATION) PROCESSOR
VISUAL QUALITY CHECK
OUTLINE CORRECTION PROCESSOR
110
SHAPE CHARACTERIZATION PROCESSOR
120
CORRELATION PROCESSOR
130
RISK INDICATION (ESTIMATE OR THRESHOLD)
DISPLAY
140
AS REQUIRED
ARCHIVAL MEMORY
150

FIG. 1

FIG.2

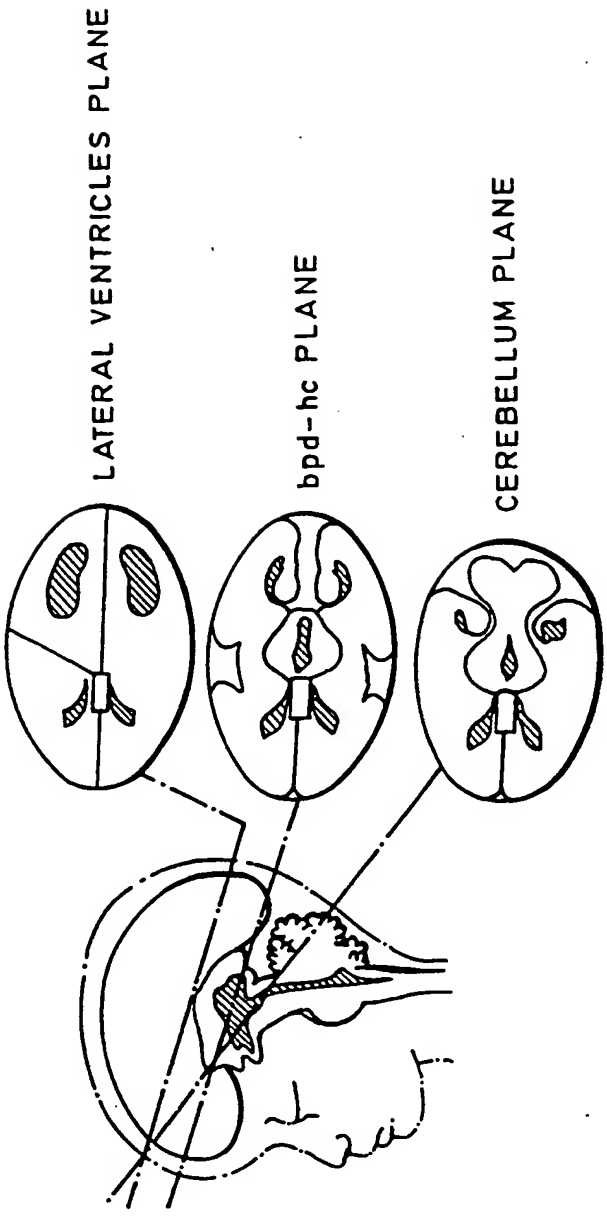


FIG. 3

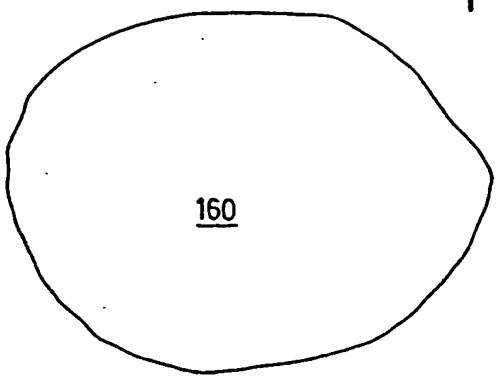
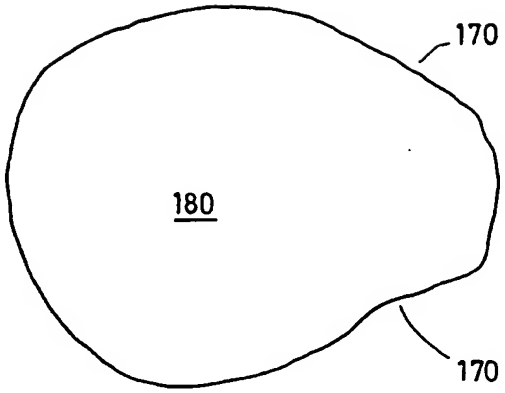


FIG. 4



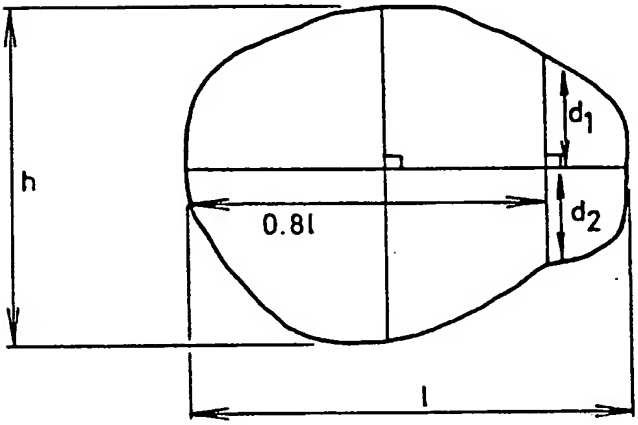


FIG. 5

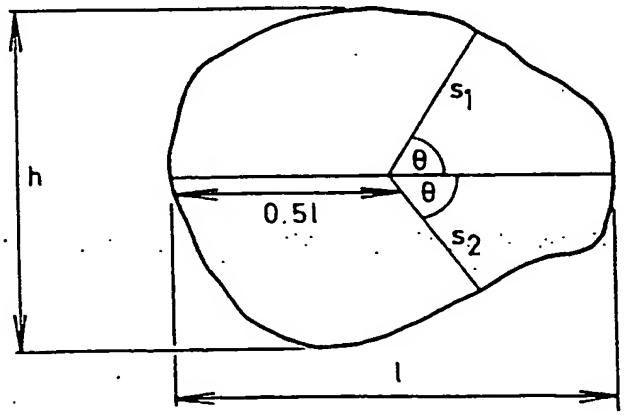


FIG. 6

FIG. 7

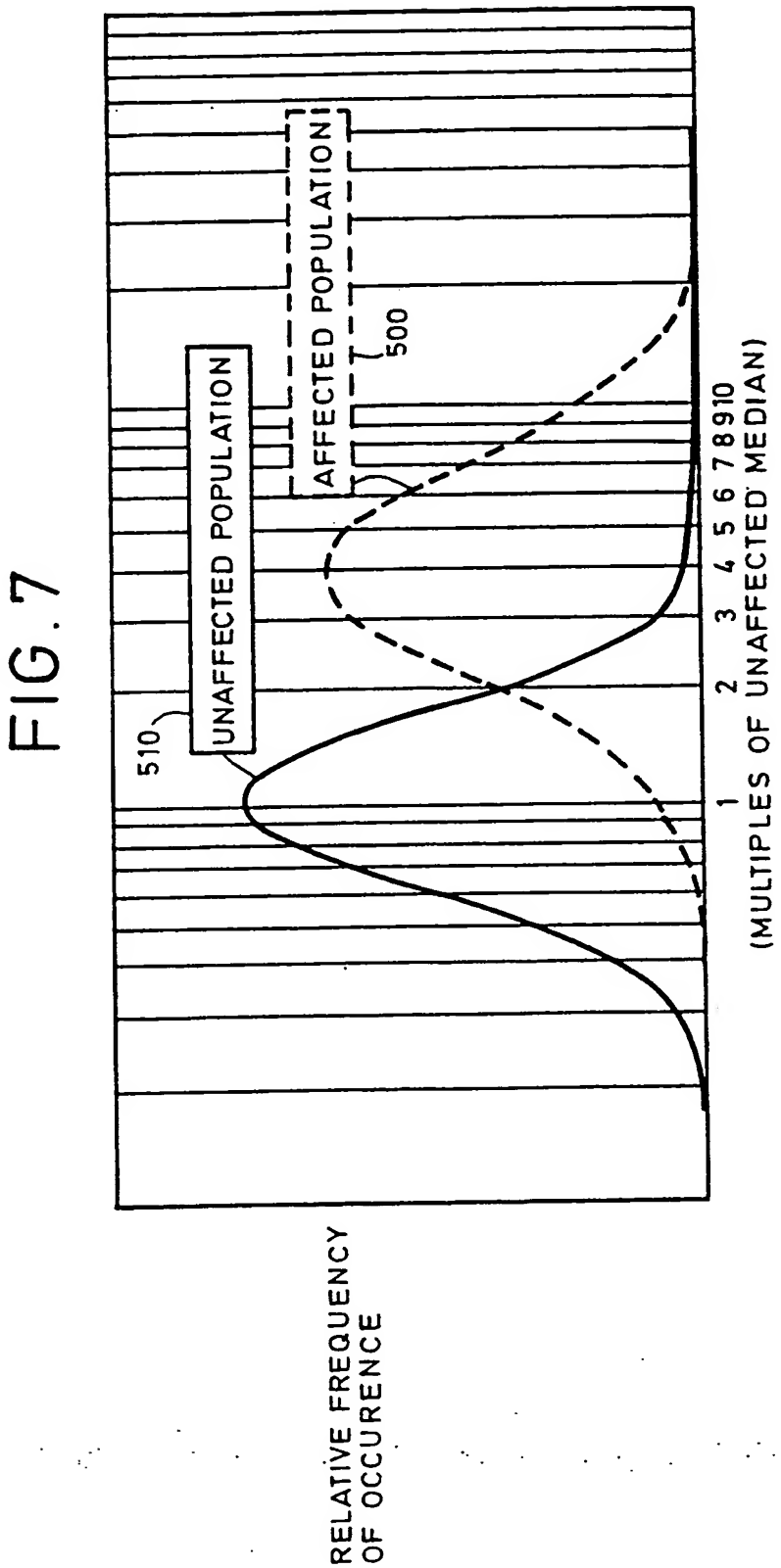
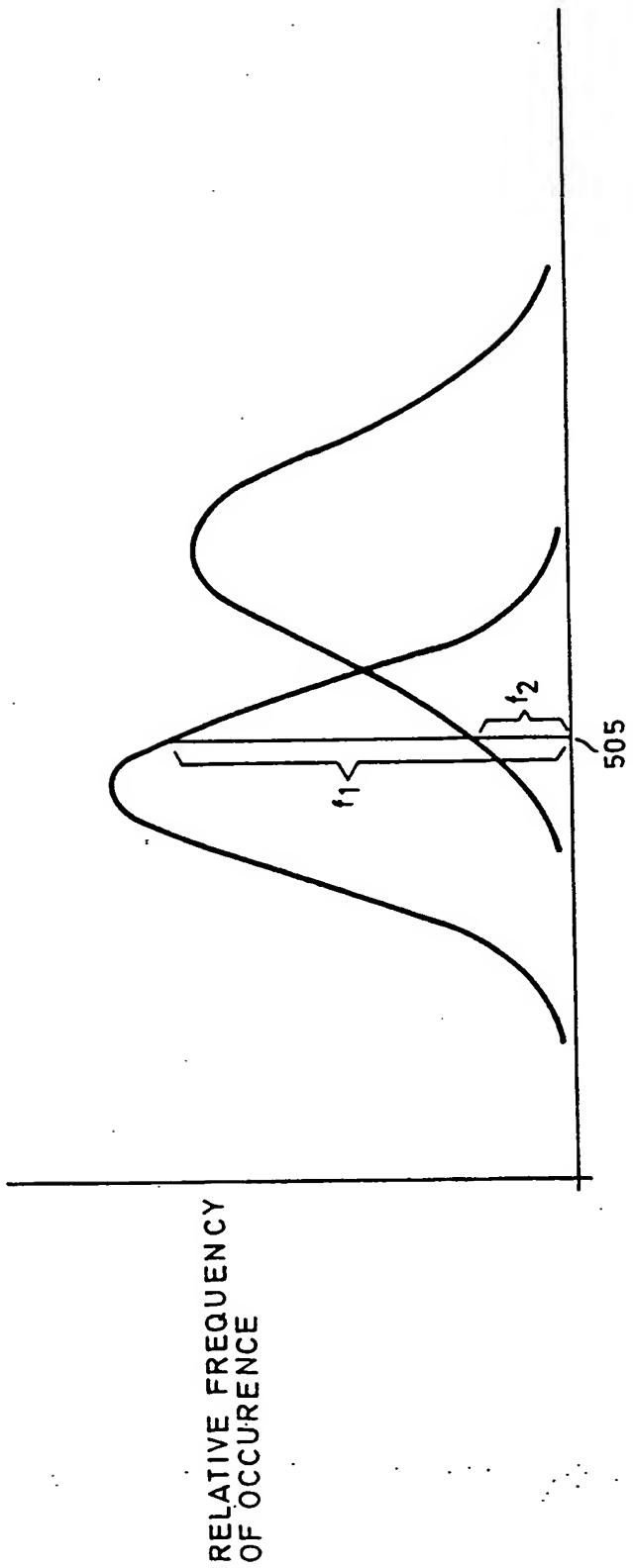

UNAFFECTED POPULATION
AFFECTED POPULATION
510
500
1 2 3 4 5 6 7 8 9 10
(MULTIPLES OF UNAFFECTED MEDIAN)
RELATIVE FREQUENCY OF OCCURENCE

FIG.8



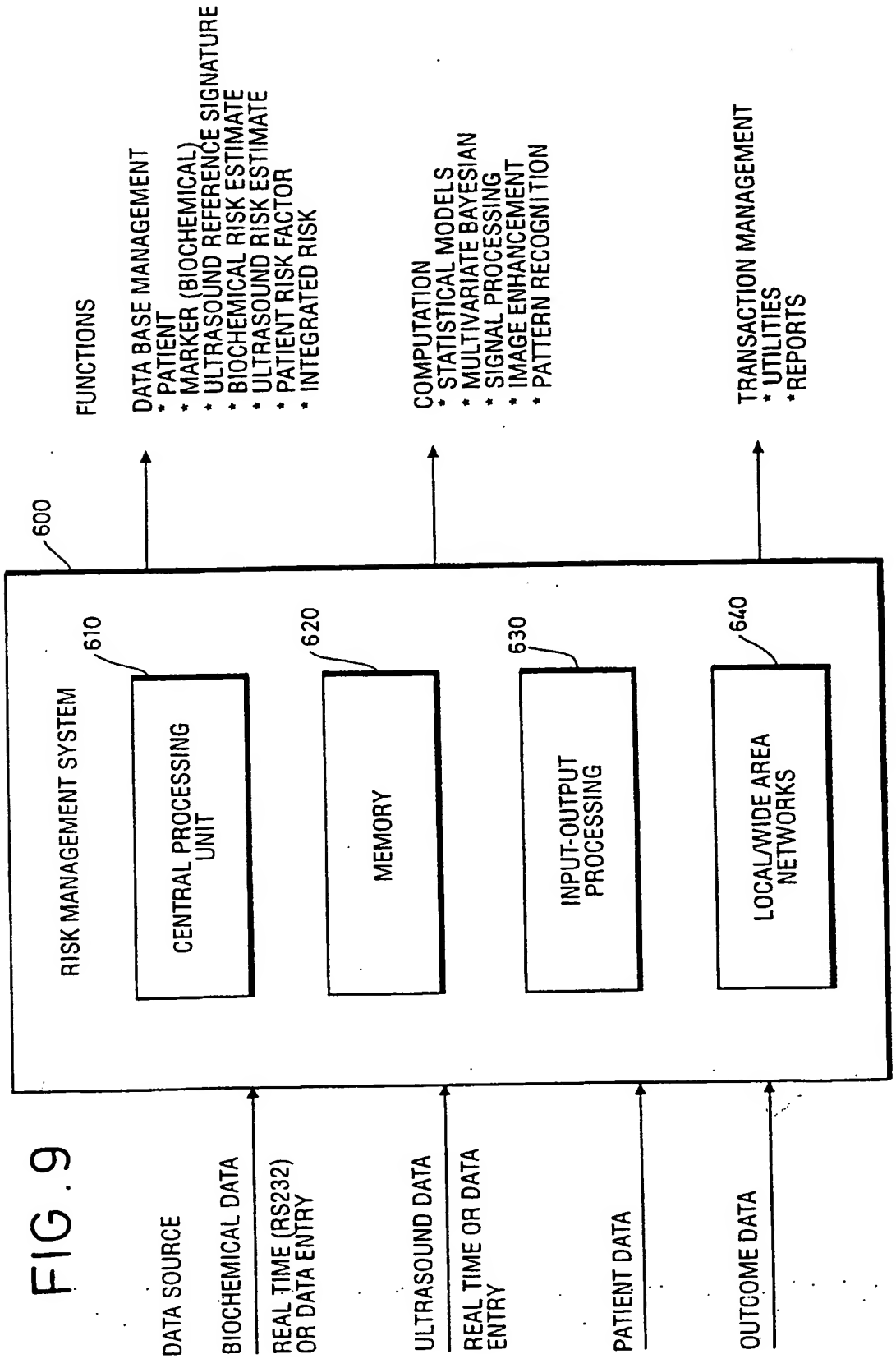

FUNCTIONS
DATA BASE MANAGEMENT
* PATIENT
* MARKER (BIOCHEMICAL)
* ULTRASOUND REFERENCE SIGNATURE
* BIOCHEMICAL RISK ESTIMATE
* ULTRASOUND RISK ESTIMATE
* PATIENT RISK FACTOR
* INTEGRATED RISK
COMPUTATION
* STATISTICAL MODELS
* MULTIVARIATE BAYESIAN
* SIGNAL PROCESSING
* IMAGE ENHANCEMENT
* PATTERN RECOGNITION
TRANSACTION MANAGEMENT
* UTILITIES
*REPORTS
600
RISK MANAGEMENT SYSTEM
610
CENTRAL PROCESSING UNIT
620
MEMORY
630
INPUT-OUTPUT PROCESSING
640
LOCAL/WIDE AREA NETWORKS
DATA SOURCE
BIOCHEMICAL DATA
REAL TIME (RS232) OR DATA ENTRY
ULTRASOUND DATA
REAL TIME OR DATA ENTRY
PATIENT DATA
OUTCOME DATA

FIG. 9

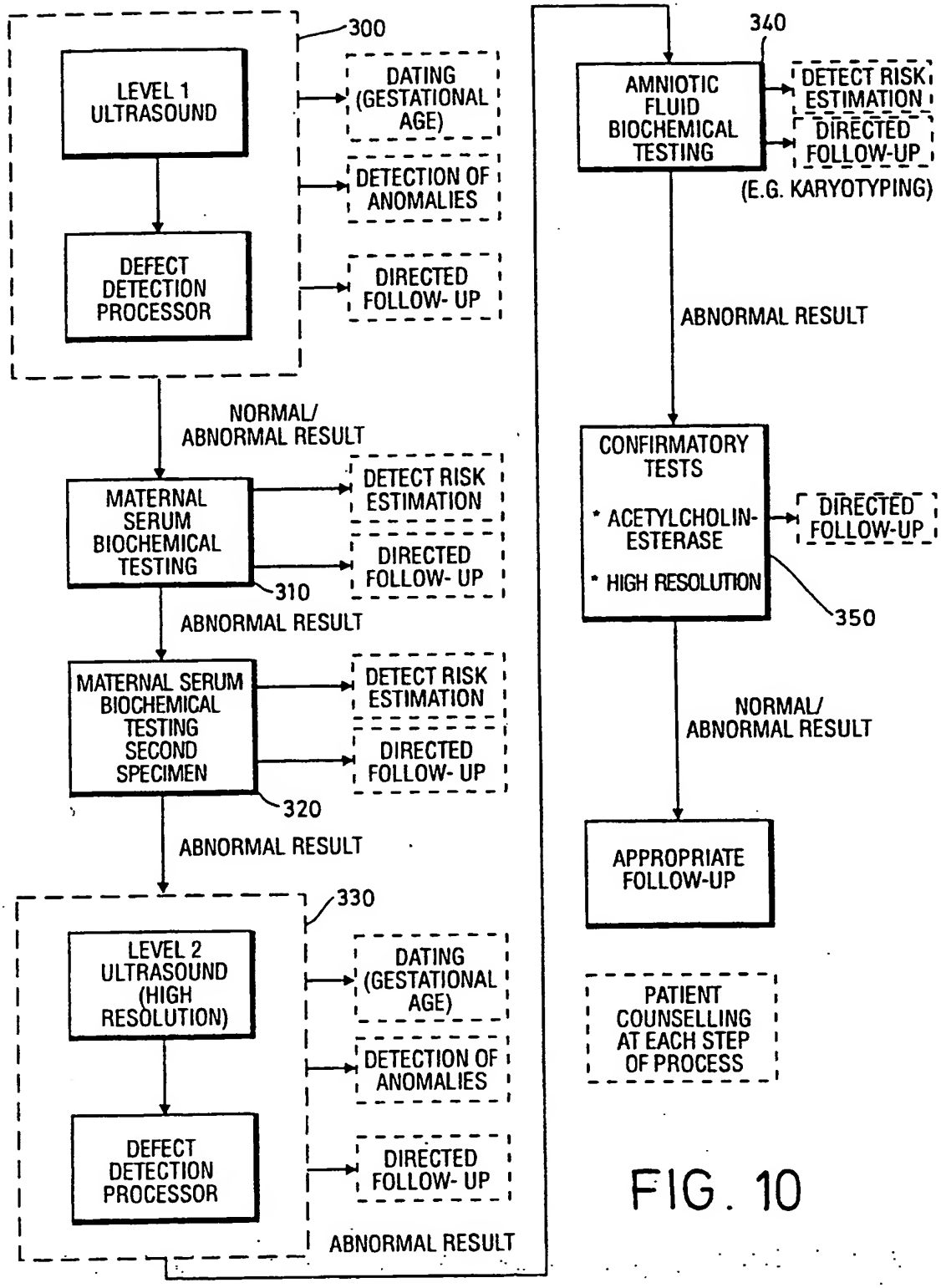

300
LEVEL 1 ULTRASOUND
DATING (GESTATIONAL AGE)
DETECTION OF ANOMALIES
DEFECT DETECTION PROCESSOR
DIRECTED FOLLOW- UP
NORMAL/ ABNORMAL RESULT
MATERNAL SERUM BIOCHEMICAL TESTING
DETECT RISK ESTIMATION
DIRECTED FOLLOW- UP
310
ABNORMAL RESULT
MATERNAL SERUM BIOCHEMICAL TESTING SECOND SPECIMEN
DETECT RISK ESTIMATION
DIRECTED FOLLOW- UP
320
ABNORMAL RESULT
330
LEVEL 2 ULTRASOUND (HIGH RESOLUTION)
DATING (GESTATIONAL AGE)
DETECTION OF ANOMALIES
DEFECT DETECTION PROCESSOR
DIRECTED FOLLOW- UP
ABNORMAL RESULT
340
AMNIOTIC FLUID BIOCHEMICAL TESTING
DETECT RISK ESTIMATION
DIRECTED FOLLOW-UP
(E.G. KARYOTYPING)
ABNORMAL RESULT
CONFIRMATORY TESTS
* ACETYLCHOLIN-ESTERASE
* HIGH RESOLUTION
DIRECTED FOLLOW-UP
350
NORMAL/ ABNORMAL RESULT
APPROPRIATE FOLLOW-UP
PATIENT COUNSELLING AT EACH STEP OF PROCESS

FIG. 10

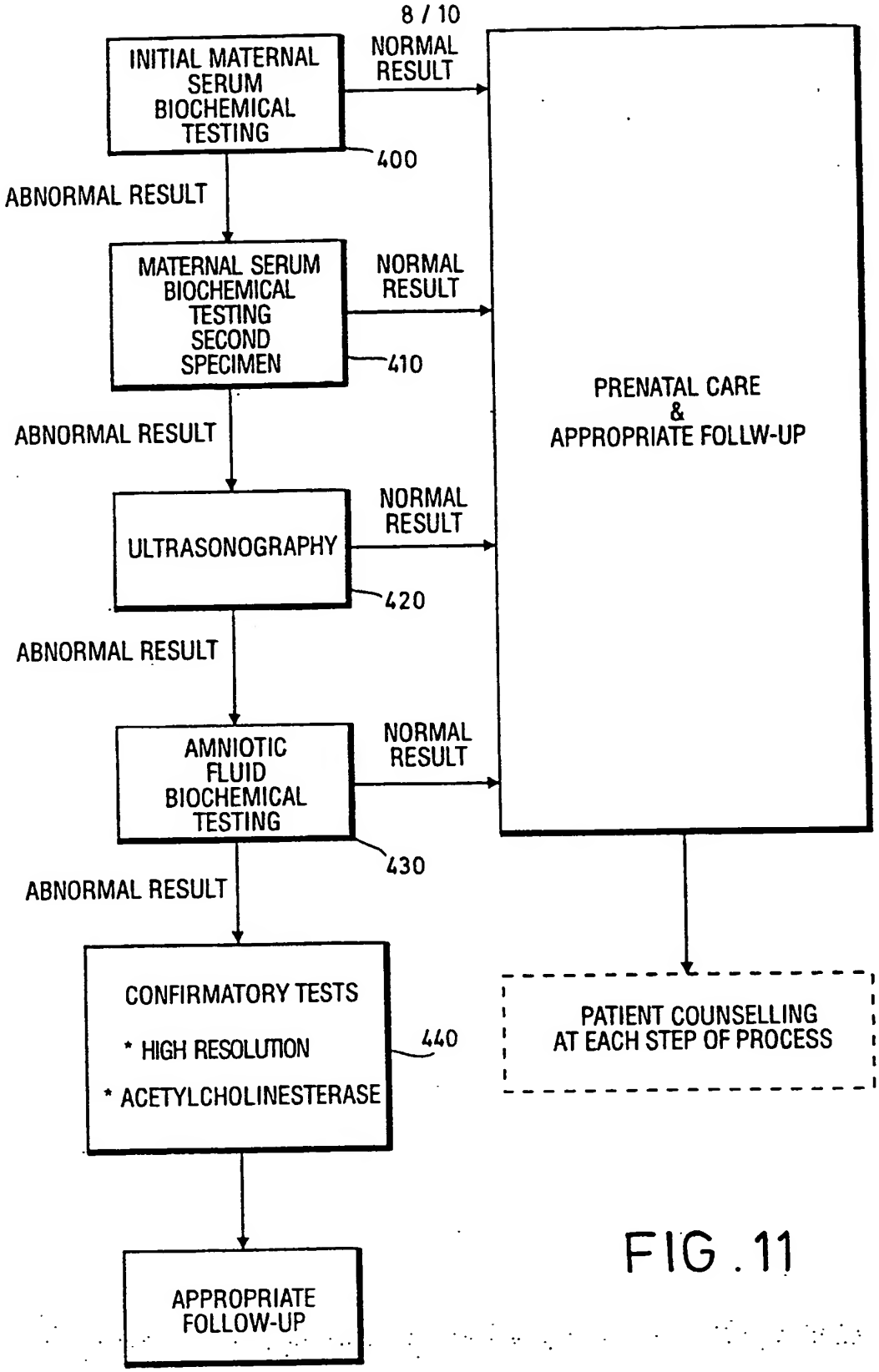

INITIAL MATERNAL SERUM BIOCHEMICAL TESTING
NORMAL RESULT
400
ABNORMAL RESULT
MATERNAL SERUM BIOCHEMICAL TESTING SECOND SPECIMEN
NORMAL RESULT
410
ABNORMAL RESULT
ULTRASONOGRAPHY
NORMAL RESULT
420
ABNORMAL RESULT
AMNIOTIC FLUID BIOCHEMICAL TESTING
NORMAL RESULT
430
ABNORMAL RESULT
CONFIRMATORY TESTS
* HIGH RESOLUTION
* ACETYLCHOLINESTERASE
440
APPROPRIATE FOLLOW-UP
PRENATAL CARE & APPROPRIATE FOLLW-UP
PATIENT COUNSELLING AT EACH STEP OF PROCESS

FIG . 11

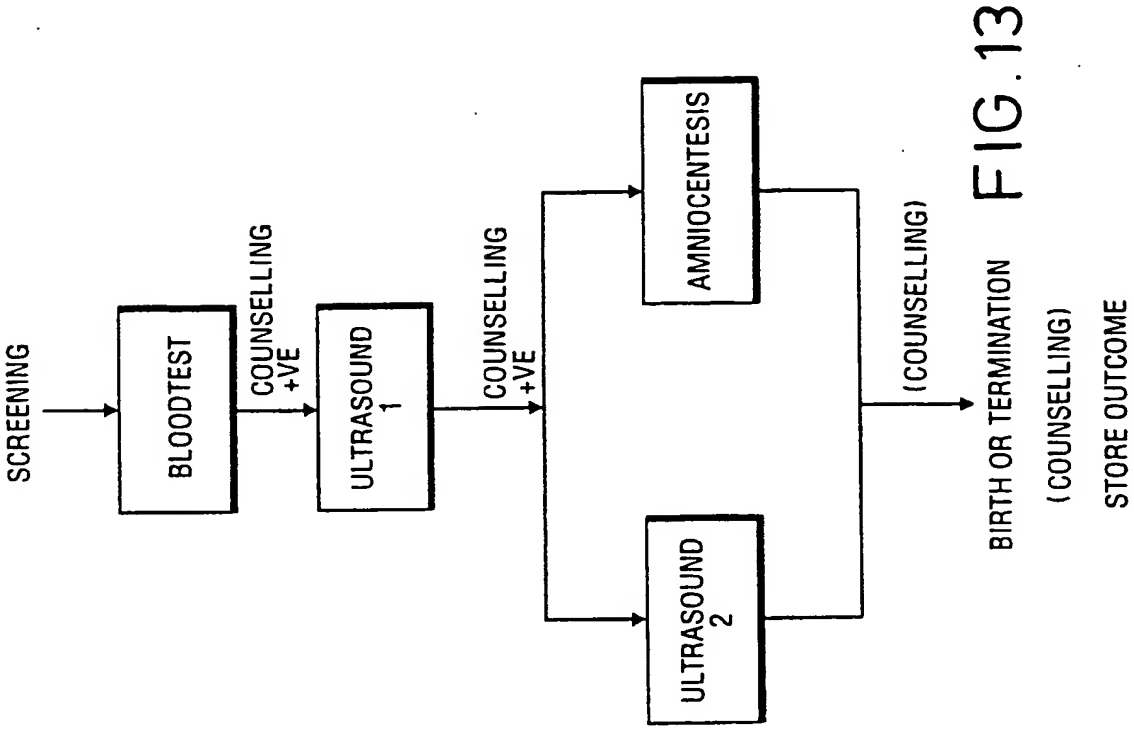

SCREENING
BLOODTEST
COUNSELLING
+VE
ULTRASOUND 1
COUNSELLING
+VE
AMNIOCENTESIS
ULTRASOUND 2
(COUNSELLING)
BIRTH OR TERMINATION
(COUNSELLING)
STORE OUTCOME

FIG. 13

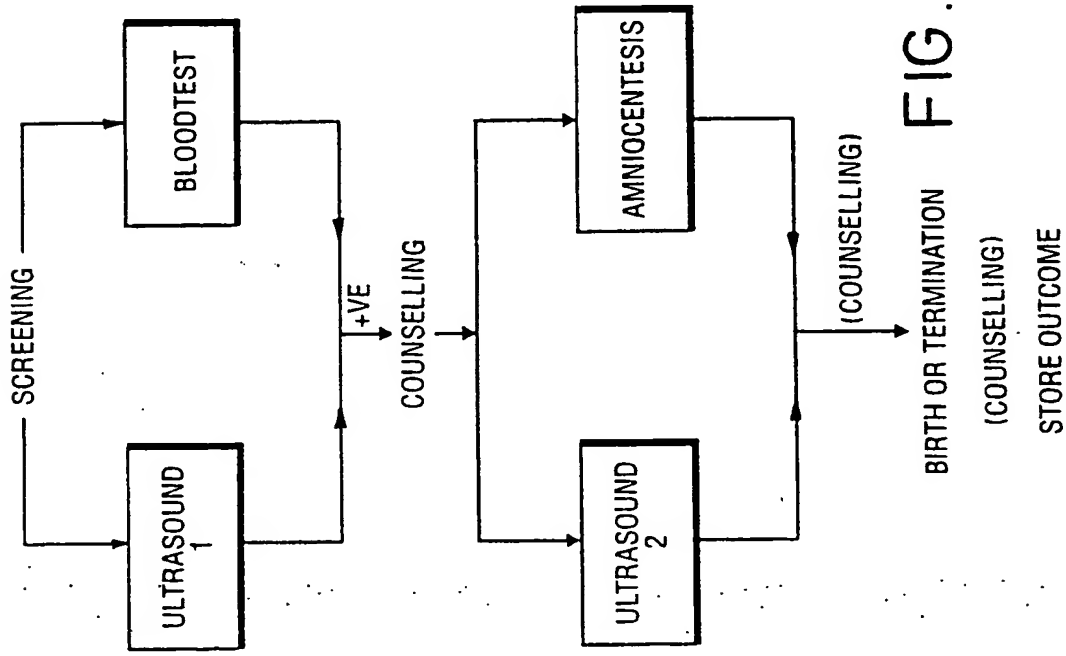

SCREENING
BLOODTEST
ULTRASOUND 1
+VE
COUNSELLING
AMNIOCENTESIS
ULTRASOUND 2
(COUNSELLING)
BIRTH OR TERMINATION
(COUNSELLING)
STORE OUTCOME

FIG. 12

FIG. 14

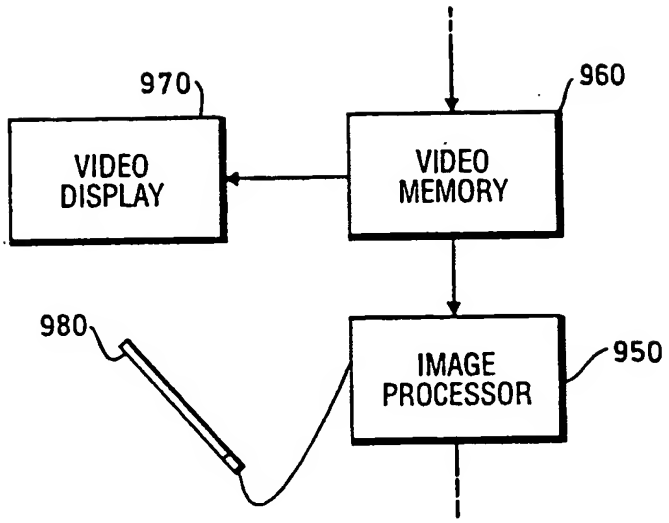
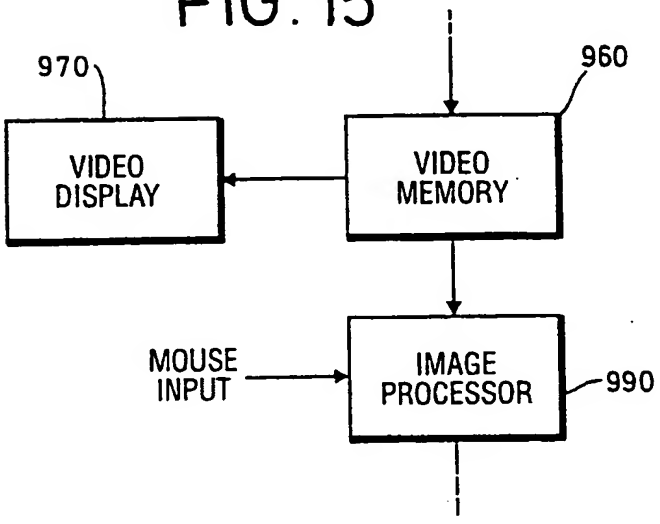

970
960
VIDEO DISPLAY
VIDEO MEMORY
980
IMAGE PROCESSOR
950

FIG. 15


970
960
VIDEO DISPLAY
VIDEO MEMORY
MOUSE INPUT
IMAGE PROCESSOR
990

INTERNATIONAL SEARCH REPORT

Internat · Application No
PCT/GB 93/02504

A. CLASSIFICATION OF SUBJECT MATTER
IPC 5 G06F15/70

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 5 G06F

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	PROCEEDINGS OF THE COMPUTER IN CARDIOLOGY MEETING 15,WASHINGTON (USA),SEPTEMBER 25-28,1988 ;IEEE CONPUTER SOCIETY PRESS ,WASHINGTON (US) pages 445 - 448 XP145698 LEE T. ANDREWS ET AL. 'An MR workstation for quantitative analysis of cardiac images' see page 445, left column, line 1 - line 6 see page 447, left column, line 1 - line 5 see page 448, left column, line 27 - line 30 --- -/--	1,2, 38-41

[X] Further documents are listed in the continuation of box C.

[ ] Patent family members are listed in annex.

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"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
13 April 1994	02.05.94

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax (+31-70) 340-3016	Chateau, J-P

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INTERNATIONAL SEARCH REPORT

Internati ' Application No
PCT/GB 93/02504

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category '	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	SYSTEMS & COMPUTERS IN JAPAN. vol. 23, no. 7 , 1992 , NEW YORK US pages 89 - 99 XP298694 TAKAMI YASUDA 'An automatic measurement for intracranial volume usong 3-d image processings' see page 89, left column, line 23 - right column, line 8 see page 92, paragraph 4.1 - page 94, paragraph 4.2; figures 13,B,D	21,22,35
A	AMERICAN SCIENTIST;SIGMA XI,THE SCIENTIFIC RESEARCH SOCIETY(US) vol. 72, no. 6 , November 1984 pages 608 - 613 JASON CORDELL BIRNHOLTZ ET AL. 'Ultrasound images of human fetal development' see page 611, left column, line 22 - line 42	1,24
A	REVUE D'éPIDéMIOLOGIE ET DE SANTÉ PUBLIQUE vol. 32, no. 1 , 1984 pages 62 - 69 WALD N.J. ET AL. 'aLPHA-fetoprotein screening for open spina bifida:effect of routine biparietal diameter measurement to estimate gestational age'	1
A	BIO-MEDICAL ENGINEERING(GB) vol. 9, no. 7 , 1974 pages 290 - 295 FLEMING J.E.E. 'The design of a new system for ultrasonic foetal cephalometry' see the whole document	1
A	BRITISH JOURNAL OF OBSTETRICS AND GYNAECOLOGY vol. 87, no. 3 , March 1980 pages 219 - 221 WALD N. ET AL. 'small biparietal diameter of fetuses with spina bifida:implications for antenatal screening' see page 221, left column, line 15 - right column, line 9	1,14,17, 24-26, 29,34, 39-42, 45-48, 57, 59-66, 75,77